IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

10X GENOMICS, INC., and THE BOARD OF TRUSTEES OF LELAND STANFORD JUNIOR UNIVERSITY, Plaintiffs, v. PARSE BIOSCIENCES, INC., Defendant.	C.A. No. 22-cv-1117-MN

PARSE BIOSCIENCES, INC.'S OPENING BRIEF IN SUPPORT OF MOTION TO DISMISS

Dated: October 17, 2022

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I. NATURE AND STAGE OF THE PROCEEDINGS

On August 24, 2022, Plaintiff 10x Genomics, Inc. ("10x") filed a patent infringement complaint against Defendant Parse Biosciences, Inc. ("Parse"), alleging infringement of six patents, which can be grouped into two families:

- First, there are three patents listing Jason D. Buenrostro as one of the inventors (United States Patent Nos. 10,150,995 ("the '995 patent"), 10,619,207 ("the '207 patent"), and 10,738,357 ("the '357 patent")) (collectively, the "Buenrostro patents").
- Second, there are three patents listing Sydney Brenner as one of the inventors (United States Patent Nos. 10,155,981 ("the '981 patent"), 10,697,013 ("the '013 patent"), 10,240,197 ("the '197 patent")) (collectively, the "Brenner patents").

Parse now moves to dismiss the complaint for failure to state a claim.

II. SUMMARY OF ARGUMENT

10x's complaint should be dismissed in its entirety because it is based solely on patents that claim nothing more than subject matter that the Supreme Court and Federal Circuit have repeatedly found ineligible for patenting.

As to the Buenrostro patents, the common specification admits that the claim steps pertain to nothing more than a prior art process called "tagmentation," which the patents acknowledge was so routine in the industry that it was performed using commercially available kits from major biotechnology companies, such as Illumina. If there is anything new in the Buenrostro patents, it is not an invention, but rather a ***discovery*** about naturally occurring enzymes called transposons, which are used in "tagmentation." As the Buenrostro patents explain, the inventors "hypothesized" that these enzymes would, in fact, perform their normal, natural function when applied to a particular form of DNA that exists in nature. After discovering this was true, they tried to patent the natural phenomenon by claiming its use with prior art "tagmentation." The patent does not remotely suggest the need for any special processes or components, but rather that the prior art

commercial "tagmentation" systems could be "readily adapted" for use with their discovery. The inventors' attempt to monopolize a natural phenomenon in this manner is not permitted.

The Brenner patents likewise claim ineligible subject matter, albeit not a natural phenomenon, but rather the abstract idea of using a tag to label DNA from a cell to keep track of where it came from. Like the Buenrostro patents, the Brenner patents admit that the alleged invention can be performed using "conventional" techniques—using the exact language Federal Circuit recently confirmed in the *CareDx* case establishes a violation under § 101. *See, e.g.*, *CareDx, Inc. v. Natera, Inc.*, 40 F.4th 1371, 1378 (Fed. Cir. 2022). While such admissions in the Brenner patents are enough to establish ineligibility, 10x itself has likewise has admitted over and over in a prior litigation that the Brenner patents claim nothing more than an abstract idea that, according to 10X, is no different from the Dewey decimal system or the use of serial numbers and that is "as old as the scientific method."

III. STATEMENT OF FACTS

A. The Buenrostro Patents

The Buenrostro patents pertain to a prior art process known as "tagmentation," which can be used to simplify the preparation of DNA for sequencing. "Tagmentation" makes use of an enzyme known as a transposase, a naturally occurring enzyme capable of attaching an external DNA sequence to another strand of DNA while at the same time cleaving the target DNA at the point of attachment. In "tagmentation," the transposase is outfitted with a payload of DNA sequences that are necessary for the DNA sequencer to operate properly, and then the natural activity of the transposase is exploited to introduce those sequences into the sample DNA.

At the time of filing, tagmentation was routine and conventional. As the common specification of the Buenrostro patents explain, tagmentation had long since been published and was even the subject of commercial product offerings that could be "readily adapted" for the

alleged invention of the Buenrostro patents:

> Methods for tagmenting isolated genomic DNA are known in the art (see, e.g., Caruccio Methods Mol. Biol. 2011 733: 241-55; Kaper et al, Proc. Natl. Acad. Sci. 2013 110: 5552-7; Marine et al, Appl. Environ. Microbiol. 2011 77: 8071-9 and US20100120098) and are commercially available from Illumina (San Diego, Calif.) and other vendors. Such systems may be readily adapted for use herein.

D.I. 1-1, Ex. 4 at 14:23-38

What, then, is allegedly new in the Buenrostro patents? If anything at all, it is only a natural phenomenon, namely, the ability of the transposase to perform tagmentation on so-called "open chromatin." Briefly, in chromosomes, DNA is packaged into a denser structure wherein the DNA is wrapped around a barrel-shaped protein called a histone. "Chromatin" is the combination of the DNA and histone proteins. So-called "open chromatin" refers to regions of chromatin where the DNA has been partially unwound from the histone proteins so that it can be accessed by the machinery of a cell and utilized to carry out the functions of the cell. *See generally id.* at 13:54-63 (describing the meaning of "chromatin accessibility").

In 2013, a group of researchers including the named inventors on the Buenrostro patents hypothesized that the "tagmentation" process would, in fact, work on "accessible chromatin:"

> Because transposons have been shown to integrate into active regulatory elements in vivo, we hypothesized that transposition by purified Tn5, a prokaryotic transposase, on small numbers of unfixed eukaryotic nuclei would interrogate regions of accessible chromatin.

Ex. 1 at 2. The inventors repeated this hypothesis nearly verbatim in their patents. *See, e.g.*, D.I. 1-1, Ex. 4 at 28:62-66.

After confirming that their hypothesis about this natural phenomenon was indeed correct, the inventors sought patent protection by integrating the natural phenomenon into otherwise generic patent claims that recite nothing more than the basics of "tagmentation." For example, representative claim 1 of the '207 patent is as follows:

1. A method for generating a sequencing library from a plurality of cells, comprising:

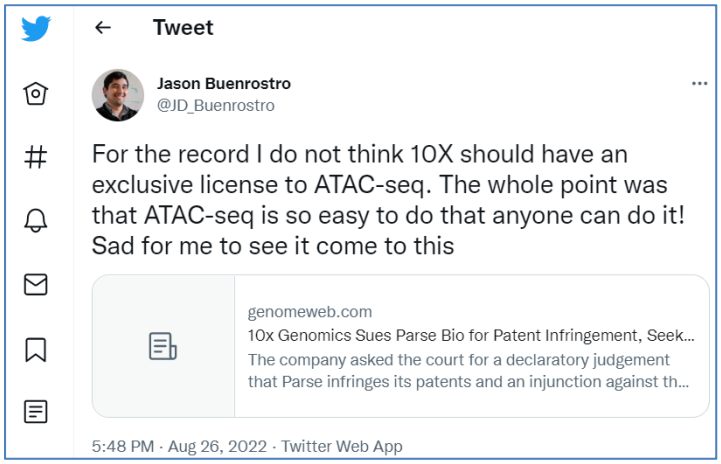
a) lysing a plurality of cells to provide a plurality of cell nuclei, wherein the plurality of cell nuclei comprises chromatin;

b) contacting a cell nucleus of the plurality of cell nuclei with a transposase complex such that polynucleotides of the cell nucleus are tagmented at regions of open chromatin to produce a plurality of tagged fragments; and

c) performing one or more nucleic acid reactions on the tagged fragment to produce a sequencing library.

D.I. 1-1, Ex. 5 at claim 1. As the claim makes clear, this is nothing more than the prior art tagmentation process applied to chromatin. In their patents, the named inventors referred to this process as "ATAC-seq," which is simply short for "Assay for Transposase Accessible Chromatin followed by high-throughput sequencing (ATAC-seq)." *Id.* at 24:38-39.

Thus, to the extent the Buenrostro patents claim anything beyond the well-known tagmentation process, it is nothing more than the natural phenomenon that a transposase would function on so-called "open chromatin." Following this lawsuit, the lead inventor on the Buenrostro patents confirmed in a Tweet that there was nothing special about ATAC-Seq:



Ex. 2.

B. The Brenner Patents

1. Technical Overview Of The Brenner Patents

The Brenner patents were developed not at 10x, but rather at a company called Population

Genetics, Ltd. in the 2009 time frame. Population Genetics has long since ceased functioning.

The Brenner patents all share an identical specification and purport to solve a problem with prior art DNA sequencing methods, which was that such prior art technologies were often only able to resolve a short stretch of DNA sequence within much larger fragments of genomic DNA:

> One limitation of the overall process stems from limitations of existing DNA sequencing technologies. In particular, if fragments in the regions of interest of the genome are longer than the lengths that can be sequenced by a particular technology, then such fragments will not be fully analyzed (since sequencing proceeds from an end of a fragment inward).

D.I. 1-1, Ex. 1 at 1:32-37. As the Brenner patents state, the "present invention removes the limitations imposed by current sequencing technologies as well as being useful in a number of other nucleic acid analyses." *Id.* at 1:45-47.

To this end, the Brenner patents describe a technique known as the "reflex method," a technique for breaking up a long sequencing project into a series of smaller individual sequencing projects, the results of which can be pieced together to generate a long stretch of DNA sequence. *See generally id.* at 16:62-19:6. This so-called "reflex" technique works by introducing multiple copies of a "reflex" sequence along a nucleic acid molecule, which can then be used to further introduce additional sequences needed for sequencing. *Id.* By introducing these sequences in close proximity to one another, one can allegedly sequence the longer DNA in bite-sized chunks. *Id.* at 17:26-33 ("Thus, each product from each reflex process can be sequenced in a single run.").

The Brenner patents are clear that this technique of introducing sequences via the "reflex" method is "the invention" itself. *See, e.g.*, *id.* at 12:52-56 ("The invention is drawn to compositions and methods for intramolecular nucleic acid rearrangement that find use in various applications of genetic analysis, including sequencing, as well as general molecular biological manipulations of polynucleotide structures."). Indeed, the "reflex" method is the very first thing mentioned in the Summary Of The Invention, and is referred to no less than ***225*** additional times throughout the

common specification of the Brenner patents. *See generally* D.I. 1-1. Every example and embodiment pertains to the "reflex" method.

Unsurprisingly, when the original inventors first sought patent protection in 2009, their claims closely tracked the "reflex" method in the specification. *See* Ex. 3. Yet, years later,10x assumed control of the Brenner portfolio, and began drafting claims that had little, if anything, to do with the "reflex" method set forth in the Brenner patents. Rather than pertaining to the "reflex" method, 10x's newly-drafted claims pertain to the concept of putting a "tag" on a DNA sequence so that one can keep track of where the DNA sample originally came from:

This concept is exemplified by representative claim 1 of the '981 patent, which is reproduced below:

> A method of analyzing nucleic acids from a plurality of single cells, the method comprising:
>
> (a) providing a sample comprising a plurality of single cells, wherein each single cell of the plurality of single cells comprises a plurality of sample polynucleotides;
>
> (b) generating a plurality of tagged polynucleotides from the plurality of sample polynucleotides, wherein each tagged polynucleotide comprises:
>
> (i) a sequence from a sample polynucleotide of the plurality of sample polynucleotides; and
>
> (ii) a multiplex identifier (MID) sequence comprising:
>
> ***I. a first tag sequence associated with the single cell from which the sample polynucleotide is derived, wherein the first tag sequence is a different sequence for different single cells in the plurality of single cells; and***
>
> ***II. a second tag sequence distinguishing the sample polynucleotide from other sample polynucleotides derived from the same single cell;***
>
> (c) sequencing the plurality of tagged polynucleotides to obtain a plurality of identified polynucleotide sequences;
>
> (d) using the first tag sequence to correlate the identified polynucleotide sequence with the single cell from which the identified polynucleotide sequence is derived; and
>
> (e) using the second tag sequence to correlate the identified polynucleotide sequence with the sample polynucleotide from which the identified polynucleotide sequence is derived.

As reflected in the bolded steps above, the claim purports to encompass introducing two "tags" to track nucleic acid molecules, the first of which tracks the particular cell the molecule came from and the second of which distinguishes the molecule from other molecules. The independent claims of the other asserted Brenner patents are little different in this regard.

Notably, the Brenner patents characterize this tracking process not as an invention, but rather as a prior art technique that the inventors had previously accomplished. *See, e.g.*, D.I. 1-1, Ex. 1 at 1:26-29 ("We have ***previously described*** methods that enable tagging each of a population of fragmented genomes and then combining them together to create a 'population library' that can be processed and eventually sequenced as a mixture.").

While the claim above includes steps related to providing a DNA sample, tagging the sample, and then sequencing the resulting DNA sample, it is undisputed that these and all other techniques used with the alleged invention are simply well-known conventional processes. The specification of the Brenner patents states as much:

> ***The practice of the present invention may employ, unless otherwise indicated, conventional techniques and descriptions of organic chemistry, polymer technology, molecular biology (including recombinant techniques), cell biology, biochemistry, and immunology, which are within the skill of the art.*** Such conventional techniques include polymer array synthesis, hybridization, ligation, and detection of hybridization using a label. Specific illustrations of suitable techniques can be had by reference to the example herein below. However, other equivalent conventional procedures can, of course, also be used. Such conventional techniques and descriptions can be found in standard laboratory manuals such as Genome Analysis: A Laboratory Manual Series (Vols. I-IV), Using Antibodies: A Laboratory Manual, Cells: A Laboratory Manual, PCR Primer: A Laboratory Manual, and Molecular Cloning: A Laboratory Manual (all from Cold Spring Harbor Laboratory Press), Stryer, L. (1995) Biochemistry (4th Ed.) Freeman, New York, Gait, "Oligonucleotide Synthesis: A Practical Approach" 1984, IRL Press, London, Nelson and Cox (2000), Lehninger, A., Principles of Biochemistry 3rd Ed., W. H. Freeman Pub., New York, N.Y. and Berg et al. (2002) Biochemistry, 5th Ed., W. H. Freeman Pub., New York, N.Y., all of which are herein incorporated in their entirety by reference for all purposes.

D.I. 1 Ex. 1-3 at 13:32-55.

2. 10x's Litigation History Related To DNA Tagging

10x has been party to at least two prior litigations involving intellectual property related to technology for tagging DNA sequences to track their origin.

(a) The Becton-Dickinson Litigation

In November 2018, Becton, Dickinson and Company ("Beckton-Dickinson) asserted seven patents against 10x. *See* Ex. 4. The seven patents named as inventors Stephen Fodor and Glenn Fu and shall thus be referred to herein as "the Fodor patents." Each of the seven Fodor patents share the title "Digital counting of individual molecules by stochastic attachment of diverse labels." As this title suggests, the Fodor patents pertain to attaching labels to DNA molecules for the purpose of tracking and counting individual molecules. And indeed, 10X alleged that the Fodor patents were "nakedly directed at the abstract idea of labeling different objects (two or more 'nucleic acid molecules', e.g., portions of DNA) with different labels ('a plurality of nucleic acid label-tags with different sequences')." Ex. 5 at 5.

At the time, 10x sought dismissal of the Becton-Dickinson complaint on the grounds that the Fodor patents claimed ineligible subject matter under 35 U.S.C. § 101. According to 10x, the Fodor patents are "directed to the abstract (and patent-ineligible) idea of using different labels to identify objects." *Id.* at 1. 10x further argued that the Fodor patents "simply take this abstract idea and attempt to limit the use of the idea to the particular technological environment of DNA (and other nucleic acids) by adding "attaching", "amplifying", and "detecting" steps and other similarly generic techniques that were well-known and conventional before 2009." *Id*. at 5.

The Becton-Dickinson matter settled before any ruling on 10x's motion.

(b) The Celsee Litigation

In May 2019, 10x asserted four Brenner patents against a small start-up company called Celsee, Inc. ("Celsee"). Two of the three Brenner patents that are at issue in this case were at issue

in 10x's previous litigation against Celsee (*i.e.* the '197 and '981 patents).

Like the Fodor patents, the Brenner patents at issue in the Celsee litigation were directed to tagging DNA molecules. 10x, for instance, characterized the Brenner patent claims as being "directed to tagging sample polynucleotides… and then using the tags to correlate sequenced molecules to their cell and polynucleotide of origin." Ex. 6 at 1. In this regard, 10x's characterization of the Brenner patent claims is the same in substance as its prior characterization of the Fodor patent claims. As 10x made clear, both sets of claims are directed to the concept of labeling sequences for the sake of tracking them and tracing them back to their cell of origin.

The Celsee litigation settled shortly before trial.

IV. LEGAL STANDARD

A § 101 inquiry is properly raised at the pleadings stage if it is apparent from the face of the patent that the asserted claims are not directed to eligible subject matter. *See Berkheimer v. HP Inc.*, 881 F.3d 1360, 1368 (Fed. Cir. 2018) ("Patent eligibility has in many cases been resolved on motions to dismiss.").

The *Alice* two-step inquiry governs this motion. *Alice Corp. Pty. Ltd. v. CLS Bank Intern.*, 573 U.S. 208 (2014). "The court must first determine whether the patent's claims are drawn to a patent-ineligible concept – *i.e.*, are the claims directed to a law of nature, natural phenomenon, or abstract idea?" *Realtime Data LLC v. Array Networks Inc., et al*., 556 F.Supp.3d 424, 431 (D. Del. 2021). "If the answer to this question is no, then the patent is not invalid for teaching ineligible subject matter." *Id.* "If the answer to this question is yes, then the court must proceed to step two, where it considers 'the elements of each claim both individually and as an ordered combination to determine if there is an 'inventive concept – *i.e.*, an element or combination of elements that is sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself.'" *Id.*

"It is well-settled that mere recitation of concrete, tangible components is insufficient to confer patent eligibility to an otherwise abstract idea. Rather, the components must involve more than performance of 'well-understood, routine, conventional activities' previously known to the industry.'" *In re TLI Commc'ns LLC Patent Litig.*, 823 F.3d 607, 613 (Fed. Cir. 2016).

V. ARGUMENT

A. 10x's Claims Based On The Buenrostro Patents Should Be Dismissed

1. *Alice* Step 1

The claims of the Buenrostro patents are directed to nothing more than the natural phenomenon that a transposon can and will behave in its normal manner with respect to so-called "open chromatin." As the Buenrostro specifications state, the inventors "hypothesized" that a commonly used transposon would indeed carry out its previously understood natural function when introduced to chromatin. D.I. 1-1, Ex. 5 at 29:60-63. While this hypothesis turned out to be correct, it is still nothing more than a natural phenomenon. *See, e.g.*, *Roche Molecular Sys., Inc. v. Cepheid*, 905 F.3d 1363, 1370–71 (Fed. Cir. 2018) ("There is no doubt that Roche's discovery of these signature nucleotides on the MTB rpoB gene and the designing of corresponding primers are valuable contributions to science and medicine. However, '[g]roundbreaking, innovative, or even brilliant discovery does not by itself satisfy the § 101 inquiry.'") (citations omitted).

There is nothing inventive beyond this phenomenon in the claims of the asserted patents. As documented above, the "tagmentation" process recited in the claims is admitted prior art. The inventors even instruct that commercially available products can be "readily adapted" for use with the alleged invention. *Id.* at 14:35-42. In other words, the alleged invention lies not in the combination of steps in the claims (which were part of prior art commercial products), but rather the natural phenomenon that the transposon will function with open chromatin.

Notably, the claims of the Buenrostro patents do not require the use of a special engineered

transposon for use with chromatin, and nowhere do the specifications suggest that the inventors needed any sort of special transposon for this purpose. Just the opposite, the independent claim of the '207 patent recites the use of any "transposon" whatsoever. Likewise, the independent claims of the '357 and '995 patents recite the use of an "insertional enzyme complex," which the specification confirms is nothing but a prior art concept that can use any transposon whatsoever:

> The term "insertional enzyme complex," as used herein, refers to a complex comprising an insertional enzyme and two adaptor molecules (the "transposon tags") that are combined with polynucleotides to fragment and add adaptors to the polynucleotides. ***Such a system is described in a variety of publications***, including Caruccio (Methods Mol. Biol. 2011 733: 241-55) and US20100120098, which are incorporated by reference herein.

D.I. 1-1, Ex. 5 at 13:23-30; *see also id.* at 15:60-16:29 (describing the "insertional enzyme" as "any enzyme capable of inserting a nucleic acid sequence into a polynucleotide," including "transposases" generally).

In circumstances such as this, courts have been clear that claims are directed to an ineligible natural phenomenon. For instance, in *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, the Federal Circuit held that patent claims directed to a technique for detecting a paternally inherited nucleic acid in the bloodstream of a pregnant woman were patent ineligible where the specification explained that "[i]t has now been discovered that foetal DNA is detectable in maternal serum or plasma samples," and that this "was a surprising and unexpected finding." 788 F.3d 1371, 1376 (Fed. Cir. 2015). It was undisputed that the inventors in *Ariosa* never "created or altered any of the genetic information" in the DNA and that the relevant "nucleic acids existed in nature" before the inventors found them. *Id.* As in *Ariosa*, the inventors of the Buenrostro patents clearly stated that the ability of a transposon to function on "open chromatin" was nothing more than a "hypothesis" regarding the natural operation of transposons, which they ultimately confirmed to be correct. Likewise, as in *Ariosa*, the inventors of the Buenrostro patents do not contend to have

invented any new forms of enzyme for use with their process, but rather simply used prior art naturally occurring transposons. The only difference between this case and *Ariosa*, if any at all, is that the inventors of the Buenrostro patents do not even characterize their discovery as "surprising and unexpected."

2. *Alice* Step 2

To the extent the claims of the Buenrostro patents are directed to a natural phenomenon under *Alice* step 1, they can satisfy § 101 only if they can survive *Alice* step 2 by reciting sufficient additional inventive elements such that the invention is "significantly more" than the ineligible abstract idea. *Alice*, 573 U.S. at 217-18. Yet, beyond capturing the ability of a transposon to work with "chromatin" the claims otherwise recite nothing other than prior "tagmentation," which, as documented above, was so routine that it was part of commercial products. *See supra* Part III.A.

Claim 1 of the '995 patent and claims 2 and 24 of the '207 patent further call for "sequencing" the sample that has been subject to the claimed method. The specification states that this can be done using "any convenient method," including the methods in three different commercial products and seven different prior art publications. *See* D.I. 1-1, Ex. 5 at 14:66-15:15. Likewise, several dependent claims recite the use of a specific type of transposon known as "Tn5." This too was nothing but a conventional well-known transposon. *Id.* at 29:55-60 ("Hyperactive Tn5 transposase (Goryshin, J Biol Chem. 1998 273: 7367-7374; Adey, A. et al. Genome Biol 2010 11: R119, loaded in vitro with adapters for high-throughput DNA sequencing, can simultaneously fragment and tag a genome with sequencing adapters (previously described as 'tagmentation')."). Similarly, dependent claims that recite the use of "barcodes" do not help confer patent eligibility because this also was a well-known and routine prior art technique that had been published two decades earlier. *See id.* at 12:38-45. Certain dependent claims further recite the use of certain sample types, divalent cations, lysing, and/or permeabilizing the cells, which are nothing but

routine and conventional laboratory techniques.[1] Claims 21-23 of the '995 patent and claims 1, 3-4 and 23 of the '207 patent recite subjecting to the nucleic acid to reactions, such as amplification reactions, which has been a routine part of biological research for decades. Claims 17-19 of the '357 patent recite adjusting the number of targeted regions, which was just a feature of prior art "tagmentation." Finally, claims 17-21 of the '207 patent recite analyzing or making a "map" of the sequenced regions of DNA. Again, however, this is nothing more than routine prior art processing. In the patents, for instance, this is done using industry-standard software using built-in parameters. *See, e.g.*, *id.* at 26:24-31 (describing the use of BOWTIE software).

In short, there is nothing in the claims beyond routine and conventional techniques, much less the required inventive concept. *See, e.g.*, *Ariosa*, 788 F.3d at 1377 ("The only subject matter new and useful as of the date of the application was the discovery of the presence of cffDNA in maternal plasma or serum."); *INO Therapeutics LLC v. Praxair Distribution Inc.*, 782 Fed.Appx. 1001, 1005 (Fed Cir. 2017) (claim for methods of administering inhaled nitric oxide gas directed to an ineligible abstract idea where the claim "does no more than add an instruction" to what was already understood as conventional methods and "the body's natural processes are simply allowed to take place"); *Cleveland Clinic Found. v. True Health Diagnostics LLC*, 760 F. App'x 1013, 1019 (Fed. Cir. 2019) ("The patents disclose that an immunoassay was a known technique for measuring protein mass and never suggest that any significant adjustments needed to be made to accommodate its use for measuring blood MPO levels. Furthermore, the specification and prosecution history plainly concede that each of the process steps was well-known in the art.") (internal citations omitted).

[1] This includes, for instance, claims 3-9 of the '995 patent, claims 23-25 and 28-30 of the '357 patent, and claims 1 and 23 of the '207 patent.

B. 10x's Claims Based On The Brenner Patents Should Be Dismissed

1. *Alice* Step 1

As documented above, when 10x was faced with a lawsuit from Becton-Dickinson based on the Fodor patents, 10x characterized the Fodor patents as being "directed at" the concept of labeling polynucleotides so that one can keep track of where they came from. 10x, for instance, alleged that the Fodor patent claims were "nakedly directed at the abstract idea of labeling different objects (two or more 'nucleic acid molecules', e.g., portions of DNA) with different labels ('a plurality of nucleic acid label-tags with different sequences')." Ex. 5 at 5.

Subsequently, 10x acquired control of the Brenner patent portfolio, and began asserting several Brenner patents in litigation. Just as with the Fodor patents, 10x has always been clear that the Brenner patents are "directed to" the concept of labelling polynucleotides so that one can keep track of where they came from:

> The Brenner method claims (from the #197, #981, and #459 patents) are directed to tagging sample polynucleotides with an oligonucleotide comprising two tag sequences, one specific to the cell of origin and one specific to the polynucleotide of origin, and then using the tags to correlate sequenced molecules to their cell and polynucleotide of origin.

Ex. 6 at 1; *see also* Ex. 7 at 2-3 ("The inventions claimed in the Brenner patents enabled the use of two polynucleotide tags: one tag that 'provides a correlation between a polynucleotide and its source' (such as, for example, the cell of origin) and another tag that can 'uniquely tag each polynucleotide in a sample.'").

Given 10x's characterizations of the Fodor and Brenner patents as being directed to the same concept, 10x cannot deny that the Brenner patents are directed to ineligible subject matter. Indeed, with respect to the Fodor patents, 10x could not have been clearer that they are directed to an ineligible abstract idea, characterizing the DNA labeling techniques claimed in the Fodor patents as being "abstract" and "as old as the scientific method:"

> ***The claims of the Fodor patents are directed to the abstract idea of labeling different objects with different labels. This concept is as old as the scientific method*** and is familiar to every student in any introductory science class—when performing an experiment, one needs a control and an experiment and will label them accordingly (whether that means written labels of "control" and "experiment" or "test 1" and "test 2" or "sample A" and "sample B" or some other form of labeling such as placing one in a green cup and one in a blue cup). Even outside of the context of scientific experiments, using different labels to differentiate and distinguish between different instances of similar objects is commonplace. For example, different instances of the same model of a television set are given different serial numbers for warrantee or recall purposes; people attending a convention are given different name tags; and different books in a library are given different classification numbers (under the Dewey Decimal System) and are assigned different International Standard Book Numbers (ISBNs) (by the Library of Congress). ***The Fodor patents did not invent this idea—they simply take this abstract idea and attempt to limit the use of the idea to the particular technological environment of DNA (and other nucleic acids) by adding "attaching", "amplifying", and "detecting" steps and other similarly generic techniques that were well-known and conventional before 2009*** (the earliest provisional application).

Ex. 5 at 4-5. Likewise, 10x characterized the Fodor patents as being directed to "the ***abstract idea*** of labeling different molecules (like DNA) with different labels:"

> Of the 11 patents asserted by BD in this case, ***the 7 patents in the "Fodor" family are directed to the abstract (and patent-ineligible) idea of using different labels to identify different objects***. They each claim, in various forms, ***the abstract idea of labeling different nucleic acid molecules (like DNA) with different labels***. Because this amounts to nothing more than an attempt to limit the application of the abstract idea to a particular technological environment (DNA and nucleic acids), the Fodor patents are directed to an ineligible abstract idea under *Mayo* step 1.

Id. at 1.

Over and over, 10x was crystal clear that the concept of labeling DNA molecules as claimed in the Fodor patents was nothing more than a patent-ineligible abstract idea:

- "The claims of the Fodor patents similarly fail under step 1 because they are directed to the long-practiced idea of labeling different objects with different labels applied in the particular technological environment of DNA (and other nucleic acid molecules)." *Id.* at 11.
- "Because more easily distinguishing between similar objects is a well-understood benefit that humans have realized from using different labels to label different

> objects for centuries, the Fodor claims are directed to an ineligible abstract idea." Ex. 8 at 1

- "There is no dispute that claims to using conventional computer programming techniques to associate different file name labels with different data files to better organize, count, or analyze those files would not be patent eligible. The Fodor patents' use of conventional lab techniques to achieve the same goals is no more eligible." *Id.*

- "Although BD argues that the Fodor claims are directed to 'a specific improvement for quantitating and detecting target molecules' BD fails to identify any improvement other than the use of different (what BD calls 'diverse') labels to label (and count) the different instances of the target molecules. This is the same 'improvement' humans have recognized from the application of this same abstract idea in contexts other than DNA for centuries: when trying to distinguish between multiple instances of similar objects (e.g., to count them) it is helpful to label each instance with a different label." *Id.* at 2 (internal citations omitted)

10x argued that its position was supported by several cases, such as *Tangelo IP, LLC v. Tupperware Brands Corp.*, No. 18-CV-692-RGA, 2018 WL 6168083 (D. Del. Nov. 26, 2018). As 10x explained, in *Tangelo*, "the court granted a motion to dismiss based on § 101 ineligibility, finding that the claims were directed to a long practiced abstract idea applied in a particular technological environment (there, a generic computer) without any added inventive concept:

> Rather, I believe the '005 patent claims are directed to the abstract idea of using an identifier to allow a reader of a printed publication to access related information not in the printed publication—the same concept long practiced by systems of sales representatives and printed product catalogs….

Tangelo, 2018 WL 6168083, at *4.

10x firmly rejected any suggestion that cases related to computer-implemented inventions were inapplicable to biology inventions, asserting that "Courts have repeatedly found DNA-related claims ineligible, including claims directly analogous to the asserted Fodor claims." Ex. 8 at 2. Not "even a single citation to any case," 10x said, supported the view that caselaw from the context of computer-implemented inventions were "inapplicable." *Id.* Just the opposite, 10x argued that

numerous cases from the software field confirmed that claims like that those that appear in the Brenner parents are ineligible under § 101:

> ***As in Tangelo, Finnavations, Intellectual Ventures, Content Extraction, and many similar cases, in this case humans have long performed the abstract idea of using different labels to label or identify different instances of an object***, including using serial numbers to distinguish between television sets, Dewey Decimal card catalogue numbers to distinguish between books in the library, labels on test tubes to distinguish between samples in an experiment, or even name tags to distinguish between attendees at a convention or meeting. ***Attempting to limit the application of that abstract idea to DNA (and other nucleic acid molecules) does not save the claims under step 1 any more than would limiting the application of the idea to the Internet or to a generic computer***.

See Ex. 5 at 12.

Given its characterization of the Brenner patents as being directed to tagging polynucleotides to keep track of their origin, and its prior positions with respect to the Fodor patents, 10x cannot credibly contend that the Brenner patents are directed to anything other than a patent ineligible abstract idea.

2. *Alice* Step 2

In its complaint, 10x does not identify any inventive concept allegedly embodied in the claims of the Brenner patents or identify any claim steps that would allegedly confer patent eligibility. Just the opposite, 10x studiously avoids any characterization of the claims of the Brenner patent, likely because it is well-aware that the Brenner patents include no inventive concept. *See generally* D.I. 1.

In fact, as documented above, the Brenner patents themselves are clear that the claims do not include any additional inventive elements because they expressly state instead that the "present invention" is performed using "conventional techniques." D.I. 1-1, Ex. 2 at 13:40-63. This language in the patents admitting that an alleged "invention" can be performed using "conventional" techniques matches ***verbatim*** the language that the Federal Circuit has held

establishes patent ineligibility. *See, e.g.*, *CareDx, Inc. v. Natera, Inc.*, 40 F.4th 1371, 1378 (Fed. Cir. 2022) (finding claims ineligible under § 101 where "patents' written description expressly states that the techniques referred to in the claimed steps are, 'unless otherwise indicated, conventional techniques of immunology, biochemistry, chemistry, molecular biology, microbiology, cell biology, genomics, and recombinant DNA, which are well within the skill of art.'").

The admission in the Brenner patents that the claims are performed using nothing but conventional techniques is not mere boilerplate, a point 10x confirmed in its litigation against Becton-Dickinson. There, 10x urged that the additional steps recited in the claims of the Fodor patents were nothing more than routine and conventional techniques. Importantly, the priority date of the Fodor patents is December 2009, which is just a few months after the earliest possible August 2009 priority date of the Brenner patents. Therefore, barring an absurd argument from 10x that there were major technological changes in the field during the four month window between August and December 2009, 10x must agree that anything it previously characterized as routine and conventional with respect to the Fodor patents is also routine and conventional with respect to the Brenner patents. As shown below, this establishes that there is no inventive concept anywhere in any claim of the Brenner patents.

For instance, certain claims in the Brenner patents recite the use of DNA sequencing, amplification, and ligation.[2] Such techniques, 10x repeatedly said, were "generic," "routine," "well-known" and "conventional:"

- "Instead, the claims recite only the abstract labeling idea together with ***generic, routine, well-known*** laboratory techniques for working with DNA and other nucleic acid molecules (like ***attaching, hybridizing, amplifying, detecting, and***

[2] This includes claims 1, 2, and 5 of the '981 patent, claims 1 and 4 of the '013 patent, and claims 1, 2, 5, and 9 of the '017 patent.

sequencing)." Ex. 5 at 12.

- "'***Amplifying***' DNA and other nucleic acid molecules is similarly described as known and the specification lists numerous example ***conventional amplification*** techniques." *Id.* at 13.
- "Claim 1 of the 808 and 502 patents additionally claim 'sequencing' steps. The Fodor patents similarly admit that ***sequencing was known and conventional***." *Id.* at 15.
- "The 'attaching' step is repeatedly described as being accomplished through '***ligation,' a technique the Fodor patents admit was known***." *Id.* at 13.

As to the use of PCR, a particular amplification method that is recited in claim 6 of the '981 patent and claim 11 of the '197 patent, 10x confirmed that this was also "indisputably routine." Ex. 8 at 8 ("Indeed, amplification using PCR is specifically claimed and PCR was indisputably routine at the time of the Fodor patents."). According to 10x, even the specific concept of using tagging in conjunction with sequencing was a previously used conventional idea. *See* Ex. 5 at 13 ("In fact, the specification admits that tags (i.e., labels) have previously been used in combination even with "next-generation sequencing methods"—a procedure that requires attaching the tags, amplifying the DNA, and then sequencing (and thus detecting) the DNA.").

Nothing else in any of the claims helps establish an inventive concept. Certain claims recite tagging by hybridizing a primer to a sequence and extending the primer, including claims 7 and 8 of the '019 patent and claims 3 and 7-8 of the '013 patent. 10x likewise characterized this concept as known and used such that it added nothing to help confer patent eligibility. *Id.* at 15 (The "specification admits such 'hybridization' techniques, as well as PCR that involves binding and extending primers, were known and were used with label tags.").

Claim 5 of the '013 patent and claim 10 of the '917 patent claim on oligo dT sequence for use in tagging. Again, 10x was clear that this was "known and conventional." *Id.* at 15 ("Claim 1 of the 809 patent claims, apart from the abstract labeling idea, 'an oligo dT sequence' and 'a

sequencing primer binding site' but again the Fodor patents admit the use of oligo dT sequences and primer binding were known and conventional.").

Claim 9 of the '013 patent and claim 20 of the '197 patent of the Brenner patents recite the "random" attachment of tags to the polynucleotides. This concept, 10x said, was no more than a "mathematical abstract idea" that would not contribute to patent eligibility. *See id.* at 16 ("The dependent claims requiring attaching of the labels to be "stochastic" fail *Mayo* step 2 for the same reason—the specification admits that stochastic attachment is itself a mathematical abstract idea that was well known for more than 40 years."). *Id.* at 16 (citation omitted).

Claims 3-4 of the '981 patent, claims 2 and 6 of the '013 patent, and claims 3-4 and 25-26 of the '197 patent recite the use of various naturally occurring and routinely used sample types, such as DNA, RNA or mRNA. The use of such standard sample forms adds nothing to the abstract idea so as to confirm patent eligibility. Claims 24-26 of the '013 patent pertain to pooling samples, which is yet another concept the patents admit is prior art. *See* D.I. 1-1, Ex. 1 at 1:26-29. Indeed, pooling samples is undisputedly routine and conventional. Claim 23 of the '013 patent and claims 23-24 of the '197 patent pertain to counting molecules, which is just another abstract idea. Claim 21 of the '013 patent and claim 22 of the '197 patent recite the use of solid supports, such as a "microscope slide," which is just a routine prior art technique. *See id.* at 11:25-36.

Finally, claims 12-18 of the '013 patent and claims 12-19 of the '197 patent recite adjusting the number of tags relative to the DNA sequences. Such processes, 10x confirmed, were nothing more than "an ineligible abstract idea that cannot save" the claims. *See* Ex. 5 at 16 ("However, the specification confirms that ratio selection is just performing math, and is thus itself an ineligible abstract idea that cannot save these claims.") (citation omitted).

VI. CONCLUSION

For the foregoing reasons, 10x's complaint should be dismissed.

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Respectfully submitted,

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